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The Current and Future State of Interventional Cardiology: A Critical Appraisal

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Key Words
Interventional cardiology · Percutaneous coronary intervention · Coronary stenting · Patent foramen ovale, closure · Valvuloplasty

Abstract
After 75 years of invasive and over 50 years of interventional cardiology, cardiac catheter-based procedures have become the most frequently used interventions of modern medicine. Patients undergoing a percutaneous coronary intervention (PCI) outnumber those with coronary artery bypass surgery by a factor of 2 to 4. The default approach to PCI is the implantation of a (drug-eluting) stent, in spite of the fact that it improves the results of balloon angioplasty only in about 25% of cases. The dominance of stenting over conservative therapy or balloon angioplasty on one hand and bypass surgery on the other hand is a flagrant example of how medical research is digested an applied in real life. Apart from electrophysiological interventions, closure ot the patent foramen ovale and percutaneous replacement of the aortic valve in the elderly have the potential of becoming daily routine procedures in catheterization laboratories around the world. Stem cell regeneration of vessels or heart muscle, on the other hand, may remain a dream never to come true.

Introduction

'A man is as old as his arteries.' This dictum of Dr. Thomas Sydenham [1] in the 17th century almost certainly included the coronary arteries of the heart. Little did he dream that, 300 years later, and after less than a half century of development, interventional cardiology could maintain the functional adequacy of coronary arteries and, consequently, of the heart itself, for many years beyond natural expectations. Currently, it is estimated that 560 billion US dollars are spent yearly on interventional cardiology (primarily coronary angioplasty) in Europe alone. An increase to 650 billion US dollars is anticipated by the end of the decade. Interventional cardiology constitutes half of all cardiology-related expenditures. Global estimates suggest an expenditure at least 4-fold that of Europe.

History

In vivo invasive cardiology can be traced back at least to the work of Hales who, in 1711, connected a vertical glass tube to the carotid artery of a live recumbent horse, allowing him to record the blood pressure and its variations during the cardiac cycle by observing the level of the blood column. However, more than 200 years elapsed before this initial step was followed by invasive cardiac procedures in humans.

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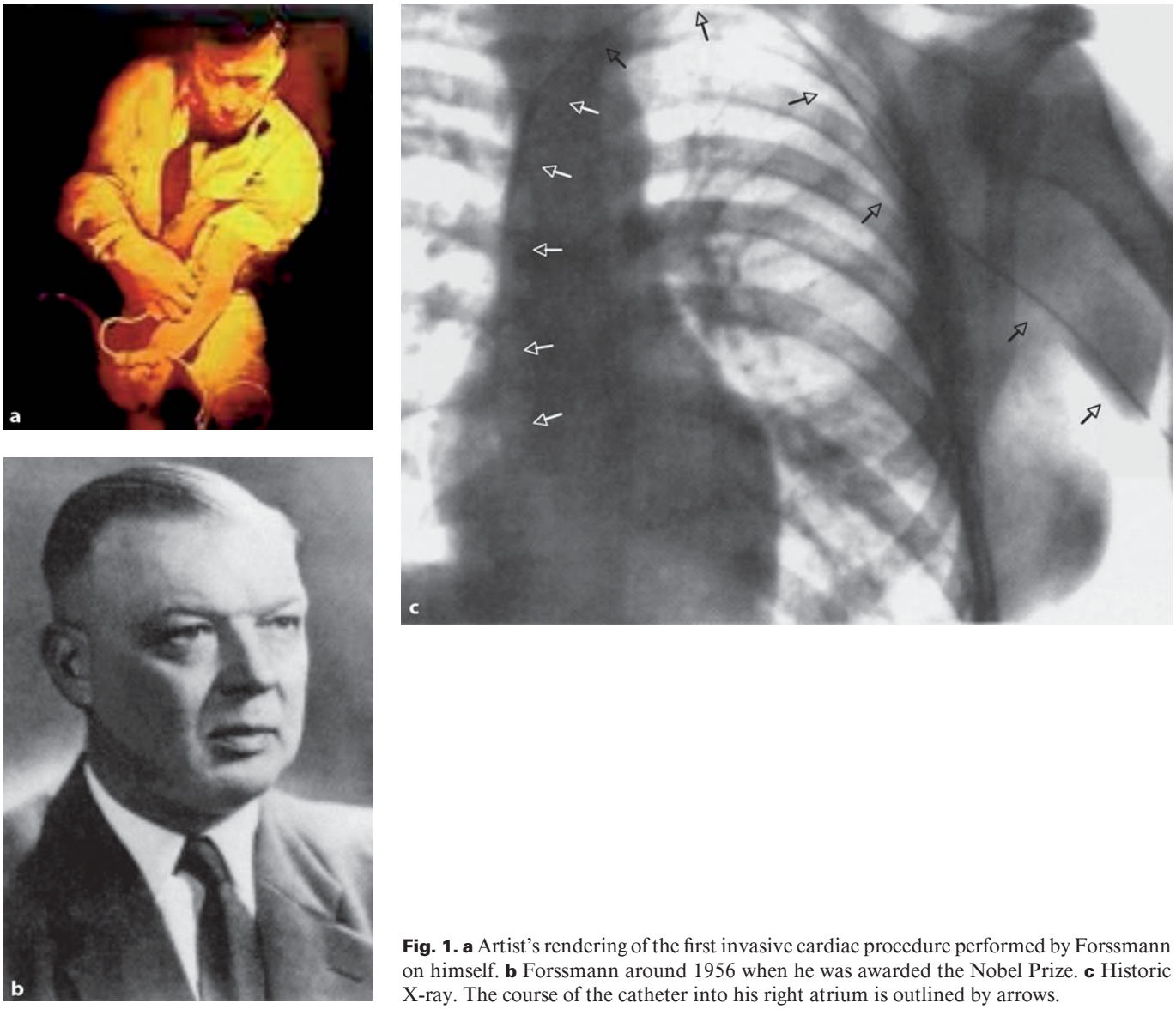

Fig. 1. a Artist's rendering of the first invasive cardiac procedure performed by Forssmann on himself. **b** Forssmann around 1956 when he was awarded the Nobel Prize. **c** Historic X-ray. The course of the catheter into his right atrium is outlined by arrows.

In 1929, Forssmann inserted a plastic urinary catheter into his own left brachial vein (performing a one-handed surgical cut-down in his elbow). He then advanced the catheter into his heart and walked the short distance to the Radiology Department (fig. 1) to document the position of the tip of the tube in his heart.

Cournand used cardiac catheterization for pressure assessments in patients to aid in the diagnosis as well as in understanding the physiology and pathophysiological changes of the human circulation. Both Forssman and Cournand were recognized for their initiative with the Nobel Prize in 1956.

Serendipity was the cradle of coronary angiography as we know it today. Sones performed the first selective coronary angiogram on October 30, 1958 by accident. This procedure has developed into one of the most common diagnostic exams in modern medicine, currently accounting for about 90% of cardiac catheterization procedures. When Sones made his breakthrough, the accepted method for visualizing the coronary arteries was to place a catheter in the ascending aorta and to perform a contrast aortogram, from which the coronary arteries were visualized indirectly. However, entry into the coronary arteries themselves, for selective angiography, was carefully avoided:

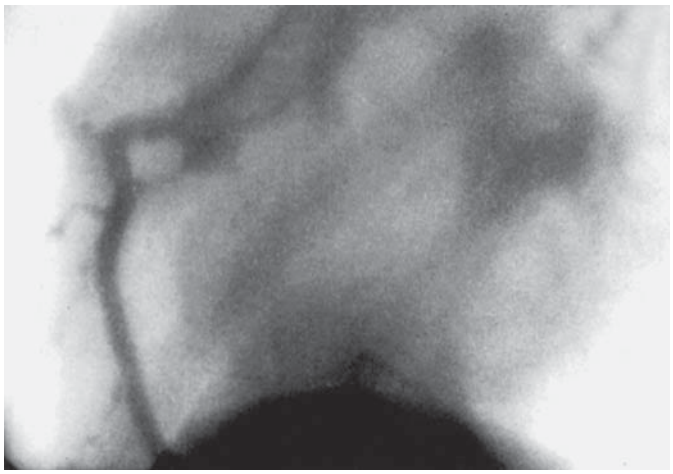

Fig. 2. First selective coronary angiogram of a right coronary artery. The aortic catheter used by Sones on October 30, 1958 had inadvertently slipped into the orifice of the right coronary artery performing a hitherto carefully avoided selective contrast medium injection.

Table 1. History of interventional cardiology

1953	Rubio-Alvarez	pulmonary wire valvuloplasty
1966	Rashkind	atrial balloon septostomy
1966	Porstmann	PDA closure
1974	King/Mills	ASD closure
1975	Gianturco	coil occlusion of shunt
1977	Gruentzig	PTCA (percutaneous transluminal coronary angioplasty)
1979	Semb	pulmonary balloon valvuloplasty (newborns)
1981	Singer	recoarctation angioplasty
1982	Kan	pulmonary balloon valvuloplasty
1982	Gallagher	His bundle ablation
1983	Lababidi	aortic balloon valvuloplasty
1984	Inoue	mitral balloon valvuloplasty
1984	Fisher	ablation of WPW pathway
1986	Puel	coronary stent implantation
1987	Simpson	coronary atherectomy (debulking)
1990	Palacios	pericardial balloon fenestration
1992	Bridges	PFO closure
1994	Sigwart	transluminal ablation of septal hypertrophy
1996	Condado	brachytherapy against coronary restenosis
1997	Oesterle	PTMR (percutaneous transmyocardial laser revascularization)
1998	Waxman	transatrial pericardial access
2000	Bonhoeffer	percutaneous pulmonary valve replacement
2001	Sievert	obliteration of left atrial appendage in atrial fibrillation
2002	Cribier	percutaneous aortic valve replacement
2003	Feldman	percutaneous mitral valve repair

ASD = Atrial septal defect; PDA = patent ductus arteriosus; PFO = patent foramen ovale; WPW = Wolff-Parkinson-White.

first, the large catheter would have blocked them off completely, theoretically associated with potentially disastrous consequences, and, second, the contrast medium then in use produced marked bradycardia even at the small doses which would be injected into the coronary arteries. Sones was appalled when he recognized during an aortic injection that the catheter had inadvertently slipped into the right coronary artery. Squatting underneath the catheterization table (as was customary at the time to observe the X-ray picture through a mirror), he saw the best resolved radiographic picture of the right coronary artery that ever had been produced up to that time (fig. 2). Asystole followed the injection but this was not sustained and ended spontaneously. This was particularly fortunate, since defibrillation, pacing, and even external cardiac massage had not been developed at the time.

Although Andreas Gruentzig is considered the father of interventional cardiology (catheter-based cardiac therapy), his first percutaneous transluminal coronary angioplasty procedure, on September 16, 1977, was preceded by more than 20 years by the report of a pulmonary wire valvuloplasty procedure by Rubio-Alvarez et al. [2] in 1953 (table 1). Moreover, in 1966, Rashkind and Miller [3] had introduced atrial balloon septostomy; this procedure is still being carried out today. Other interventional procedures relating to the heart or its adjacent vascular structures and preceding coronary angioplasty were the closure of the patent ductus arteriosus by Porstmann et al. [4] in 1966, the closure of an atrial septal defect by King et al. [5] in 1975, and the closure of arteriovenous shunts by Gianturco and colleagues [6] in 1975. These procedures have also survived in use to the present time, albeit with technical modifications.

Since, by the 1970s, coronary artery disease already accounted for the largest proportion of mortality, morbidity, and health expenditure in western countries, it is understandable that the catheter-based alternative to surgical coronary artery bypass grafting (CABG), then in use for barely a decade, created considerable interest and once and for all launched the discipline now known as interventional cardiology [7]. An assistant to the historic first procedure performed by Gruentzig on a patient who was his age-mate (38 years old), I dedicated my further professional career to this promising procedure and have had the privilege of following the first patient up to the present day. Roughly 30 years after his intervention, the

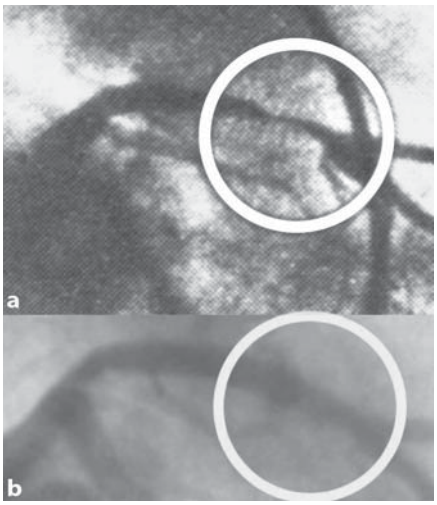

Fig. 3. Worldwide first lesion to undergo percutaneous transluminal coronary angioplasty (performed by Gruentzig on September 16, 1977 in Zürich, Switzerland) before (**a**) and 23 years after the procedure (**b**). The perfect and lasting success is apparent.

now 67-year-old pioneer patient is doing well and the lesion treated by Gruentzig was documented not to have recurred on the most recent angiogram, 23 years after the initial procedure (fig. 3) [8].

Of the many interventional cardiac procedures introduced thereafter, applied to coronary arteries or other heart structures, only two show the potential to challenge coronary angioplasty in numbers. One of them is electrophysiological ablation, introduced by Ghallager et al. [9] in 1982 with a first His bundle ablation (table 1), which certainly will be applied to large numbers of patients if current pulmonary vein isolation for atrial fibrillation becomes a standard approach for this problem. The other is closure of the patent foramen ovale, first published in 1992 by Bridges et al. [10], a procedure potentially applicable to more than 20% of the general population.

Coronary Angioplasty

Coronary angioplasty initially was called percutaneous transluminal coronary angioplasty or PTCA. More recently the nomenclature has changed to percutaneous coronary intervention (PCI). After a slow start in the late 1970s (mainly due to the fact that, at the time, coronary angiography was performed primarily in patients with severe symptoms, inadequately responsive to multidrug antianginal therapy, resulting in populations skewed to include predominantly patients with triple-vessel disease with impaired left ventricular function), procedure rates increased geometrically in the 1980s. This was not due to the widening of indications for PCI at the expense of CABG (advanced triple-vessel disease represents a poor indication for PCI to the present day) but primarily to the multiplication of catheterization facilities and a more aggressive approach to invasive evaluation, leading to earlier detection of coronary artery disease and a higher percentage of situations calling for PCI rather than CABG. Though Gruentzig had initially forecast that his technique would account for 15% of coronary revascularization procedures, before his untimely death in a plane crash in 1985, he was able to witness figures that already had exceeded this level. However, he never would have dreamt of what has happened since. Currently, in many centers, PCI is being performed 3–5 times more often than CABG (fig. 4); as a result, the predicted 15% no longer relate to PCI but rather to CABG.

An essential factor contributing to the exponential growth of PCI procedures has been the rapidly growing number of institutions offering the procedure and of operators performing it. In addition, relatively older patients have increasingly been considered eligible for PCI, with disappearing waiting lists for the procedure and the recognition that, more so than CABG, PCI usually is well tolerated even by octogenarians.

The claim is often heard that the growth of PCI procedures is due primarily to the fact that PCI has become safer in spite of progressively more risky applications. This claim is not supported by registry data. A retrospective analysis of the European PCI registry from 1992 to 2003 [11] shows that procedure-associated mortality and myocardial infarction have not decreased significantly during that interval (fig. 5). The latter finding, moreover, cannot be explained by a more aggressive approach to coronary artery disease, as the percentage of multivessel PCI performed in a single setting has remained stable during this period (fig. 6). Nonetheless, the need for emergency CABG for failed PCI procedures has fallen (fig. 5). There are several reasons: first, it is now recognized that emergency CABG for small or medium-sized coronary arteries with abrupt or impending closure does not improve the overall prognosis of the patient; second, in patients already at dire risk because of large coronary artery occlusion caused by PCI, mortality is 50% or higher even if immediate coronary bypass surgery is applied. In addition to the revision of indications for emergency CABG,

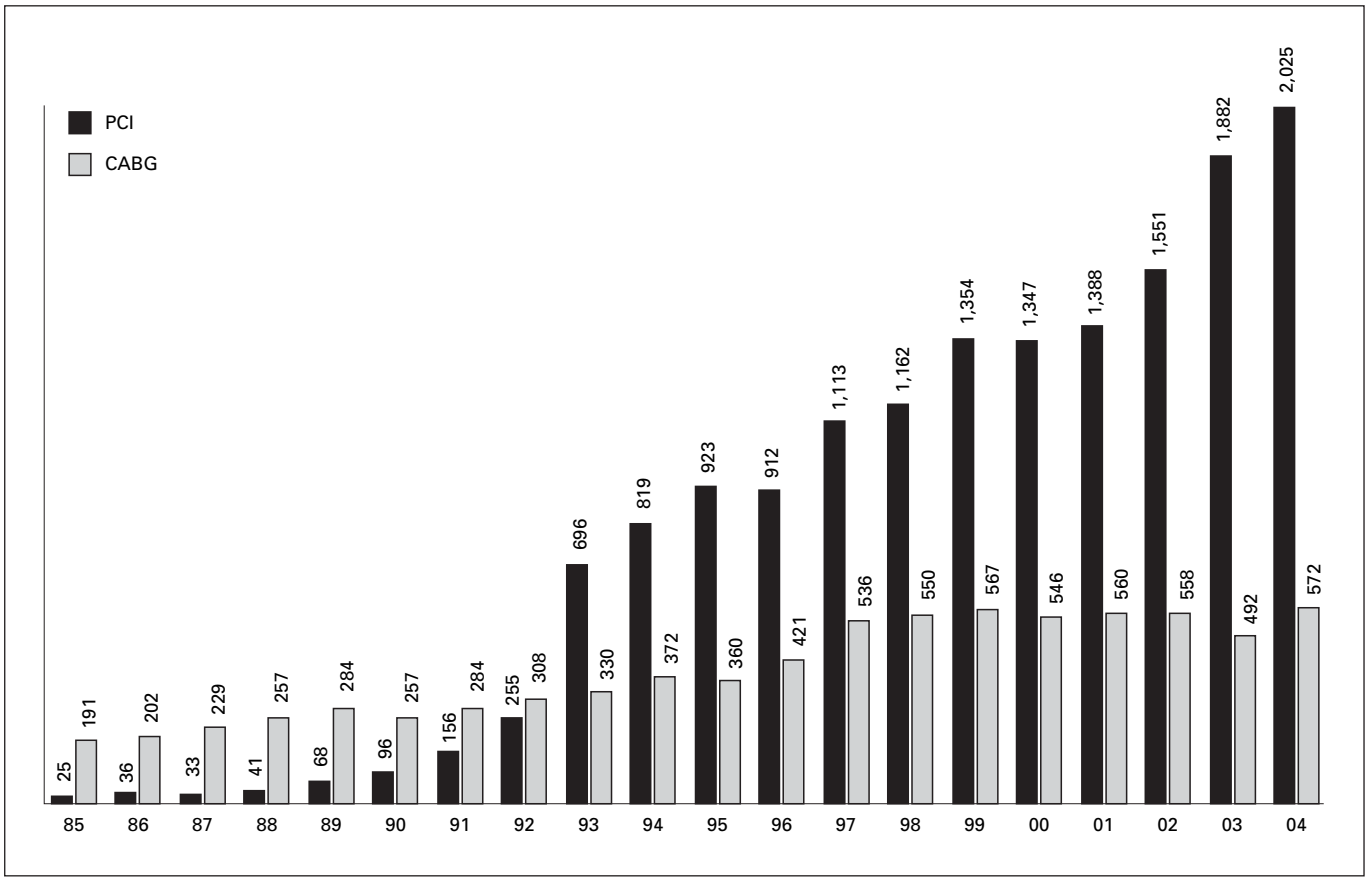

Fig. 4. Number of coronary revascularization procedures from 1985 to 2004 at the institute the author joined in 1992. After a slow start in the 1980s, PCI is now prevailing over CABG by an increasingly large margin.

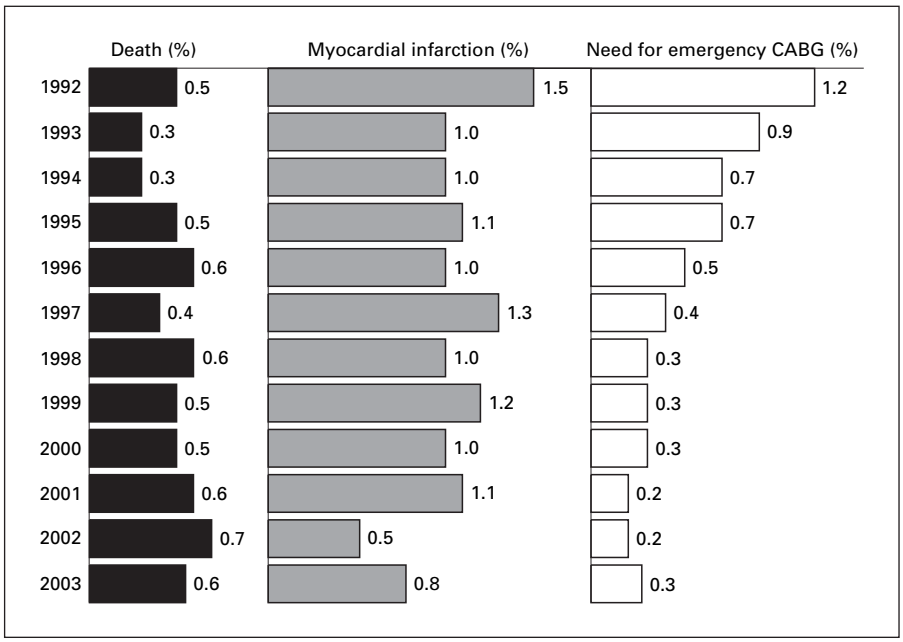

Fig. 5. Rates of death, myocardial infarction, and need for emergency CABG in a European registry encompassing a population of over 500 million people [11]. Only the need for emergency CABG showed a clear reduction over time.

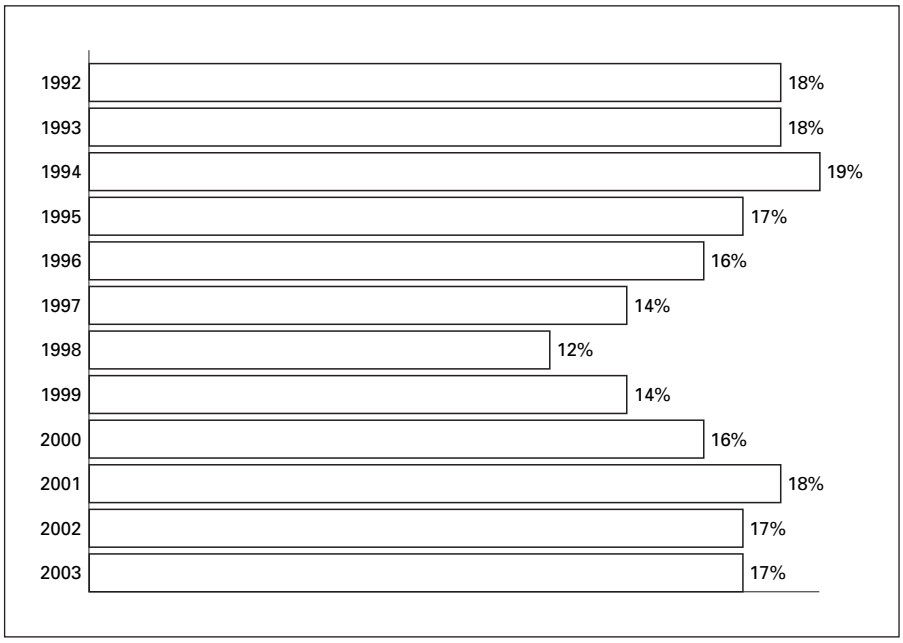

Fig. 6. Percentage of multivessel procedures in a single session per all PCI procedures in a European registry encompassing a population of over 500 million people [11]. There is no increase over time.

the introduction of the coronary stent in the late 1980s [12] provided a remedy for many previously untreatable coronary artery closures (impending or occurred) without surgery.

Numerous additions or alternatives to balloon angioplasty have been proposed during the past 3 decades. Only the introduction of stenting has proven of real value as a complement to the balloon. Introduced in 1986 (table 1) [12], it was nonetheless not an immediate success, mainly because of a misinterpretation of the initial data. At first, the stent was used only as a 'bailout' device, once a balloon procedure had caused an abrupt closure or a menacing dissection. Consequently, during that early era, outcomes of patients treated with stents were decidedly worse than those of patients treated with balloon angioplasty only. Taken at face value, these data did not account for the fact that the outcome in stented patients was likely to have been much more dismal had stents not been available. The stent's virtues of preventing abrupt closure and reducing restenosis by eliminating elastic recoil were appreciated only when randomized studies became available. Regrettably, the community of interventional cardiologists again misinterpreted the results and went to the other extreme: stenting has become the 'default' procedure, used now as the primary approach to angioplasty. This convention blatantly ignores the fact that a least 70% of balloon angioplasty procedures performed without the use of stents had excellent long-term results, without abrupt closure or restenosis. In this majority of patients, stenting is at best neutral and possibly detrimental. Subtracting about 5% (stent failures) from the 30% that theoretically could benefit from stenting in addition to balloon angioplasty, a stenting rate of about 25% appears ideal based on current data. Of course, this strategy presupposes that patients needing stents can be reliably predicted. The fact that they cannot be predicted is the basis of the argument by stent protagonists that stenting should be performed during all angioplasties.

Another factor mitigating the tendency to apply stenting to all patients is the observation that about 2% of implanted stents result in subacute or late thrombosis (a greater hazard to the patients' lives than even abrupt coronary artery closure in the catheterization laboratory). This negates the uncontested mortality reduction during the acute hospitalization achieved by the introduction of coronary stenting compared with balloon angioplasty alone (fig. 7) [13, 14]. Furthermore, while usually keeping the main vessel patent, stents engender a much higher number of side branch closures and distal embolizations of plaque fragments causing slow peripheral blood flow than does balloon angioplasty alone. This increases the risk of 'infarctlets' accompanying the procedure. A seminal meta-analysis of 29 trials encompassing about 10,000 patients randomized to either balloon angioplasty or stenting revealed that the advantage of stenting in terms of death or myocardial infarction was lost when stenting

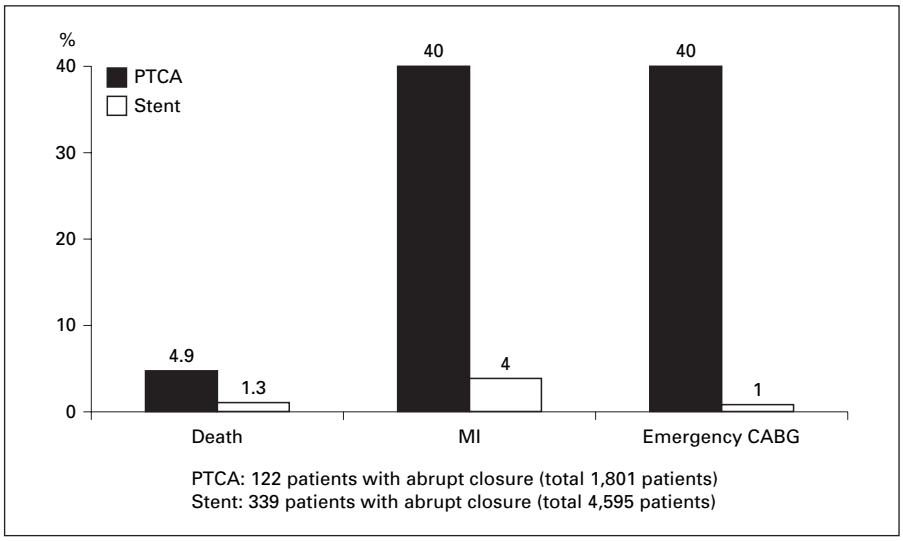

Fig. 7. Death, myocardial infarction (MI), or need for emergency CABG in patients with abrupt closure during PCI without (percutaneous transluminal coronary angioplasty, PTCA) and with the use of stents [13, 14]. The advantage of stenting is apparent.

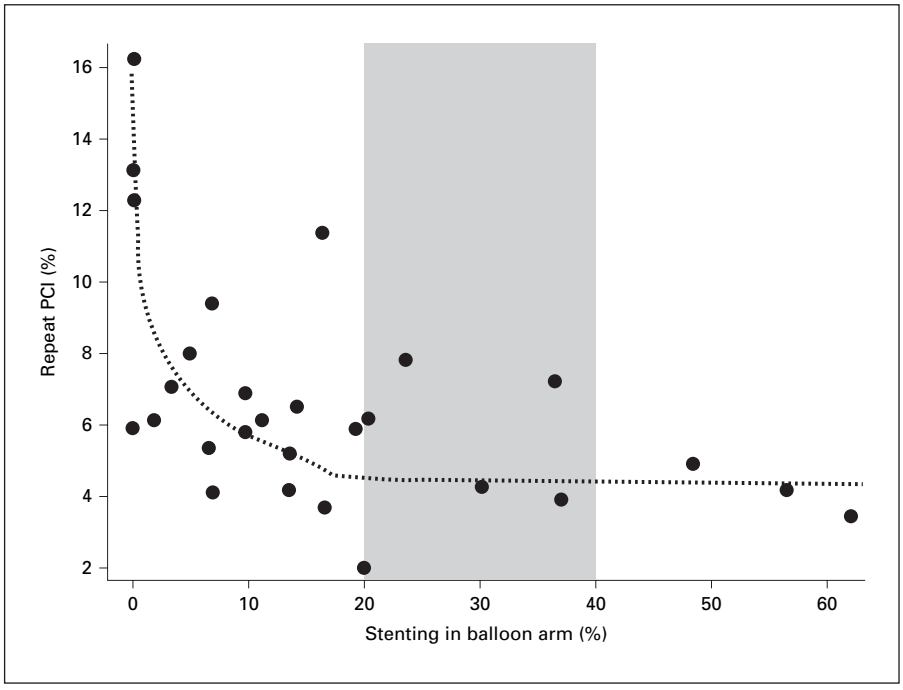

Fig. 8. Reduction of need for repeat PCI (dotted line) relative to the percent of stenting used in the balloon arm of 29 trials randomizing 9,918 patients to either balloon angioplasty or elective stent implantation [15]. The conclusion of this meta-analysis was that 'the ideal rate for stenting is difficult to determine, but our analysis suggests diminishing returns once a provisional stenting rate exceeds approximately 20 to 40%' (shaded area).

was used as a default procedure [15]. What remained was a reduction in the need for repeat angioplasty, mainly due to prevention of elastic recoil and constrictive remodeling during scarring and occurring in spite of accentuated intimal proliferation on a stented surface. However, the bulk of reduction in need for repeat angioplasty is achieved by a stenting rate of 20–40% (fig. 8). The introduction of active (drug-eluting stents) further reduces the need for repeat interventions and therefore shifts the reasonable use of electing stenting to somewhat higher percentages. Yet even the drug-eluting stents have failed to impact beneficially on prognostic endpoints, such as mortality or myocardial infarction [16]. Moreover, compared with bare metal stents, active (drug-eluting) stents may have an increased potential for late stent thrombosis, either due to the fact that the foreign body is covered by new endothelium more slowly and less completely, or due to the thrombogenicity of the polymer used in most of the active stents to slowly release the active drug.

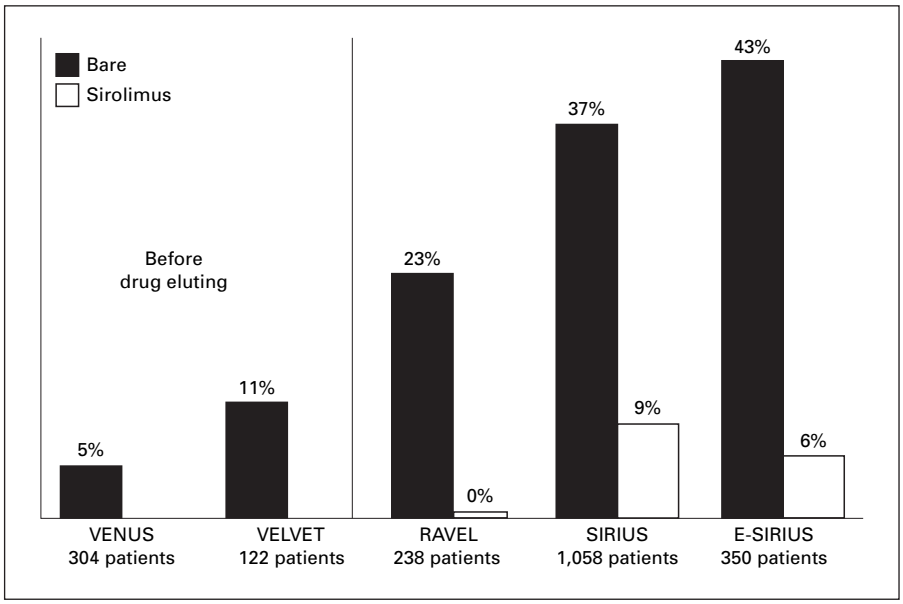

Fig. 9. Restenosis rate with the bare Bx Velocity coronary stent when compared with balloon angioplasty (to the left of the white line) and to its new sibling, the Sirolimus-eluting Cypher stent. The initially favorable percentages of the VENUS and VELVET trials increased dramatically and inexplicably, once the improved version (Cypher stent) was available (RAVEL, SIRIUS, E-SIRIUS trials), although the examined patient cohorts were comparable.

It is often surprising how much bias is involved in the interpretation of data by the community of interventional cardiologists (and, indeed, probably all physicians). First the data are usually presented in an unbalanced fashion. As long as a method is new, its virtues are overemphasized and its shortcomings are downplayed to make it appear a conspicuous improvement over the conventional technique. Once it has become the conventional technique and is then compared with a new technique or the next generation application of the same technique, its true face is revealed or even made uglier than it is in reality, again with the purpose of making the new method appear more attractive than it really is. This principle is apparent with the evolution from balloon angioplasty to stenting and then to active stenting. The need for reintervention or the recurrence rate (comfort items, not significantly impacting on prognosis) was aggravated in its importance to emphasize the relevance of differences. The restenosis rate was cited at around 30% for balloon angioplasty when no alternative existed. When stents appeared, balloon angioplasty suddenly was cited with a recurrence rate of 50%, which created a much larger discrepancy compared with an initially claimed recurrence rate of 10% for bare or passive stents. When active stents were introduced, the record of passive stents was immediately corrected to a recurrence rate of 20–40% (much in the realm previously attributed to balloon angioplasty). Again, this made active stents look more attractive with their recurrence rate of 10% or less. Figure 9 depicts this tendency with the example of the passive Bx-Velocity stent and its active sibling, the Cypher coronary stent. While it is basically condemnable to present data in a skewed fashion, it is part of human nature to react better to overstated arguments and to be rather oblivious to subtle differences. Hence, such a behavior has to be accepted as a necessity to keep research flowing and progress continuing.

In the long run, only true improvements prevail, while false progress has no future, irrespective of the strength of its initial advocacy as true progress. This has been shown repeatedly in the case of PCI (fig. 10).

After a number of years with a slowed growth of PCI procedures due to the market being close to saturated, the unconditional use of default active stenting promises a further rise in the numbers of procedures. However, in contrast to what is generally cited, this is less due to a more daring approach to coronary artery disease with PCI (remember, stenting or active stenting has not made the procedure safer) than to a less restrictive application of the procedure to early disease, i.e. hemodynamically nonsignificant lesions.

An indiscriminate use of more and ever longer active stents will make the procedure more hazardous, as subacute stent thrombosis (associated with a mortality of about 50%) will invariably increase with every millimeter of stent implanted, even if the suspected higher propensity of active stents for such late complications compared with the passive stents remains a myth or can be elimi-

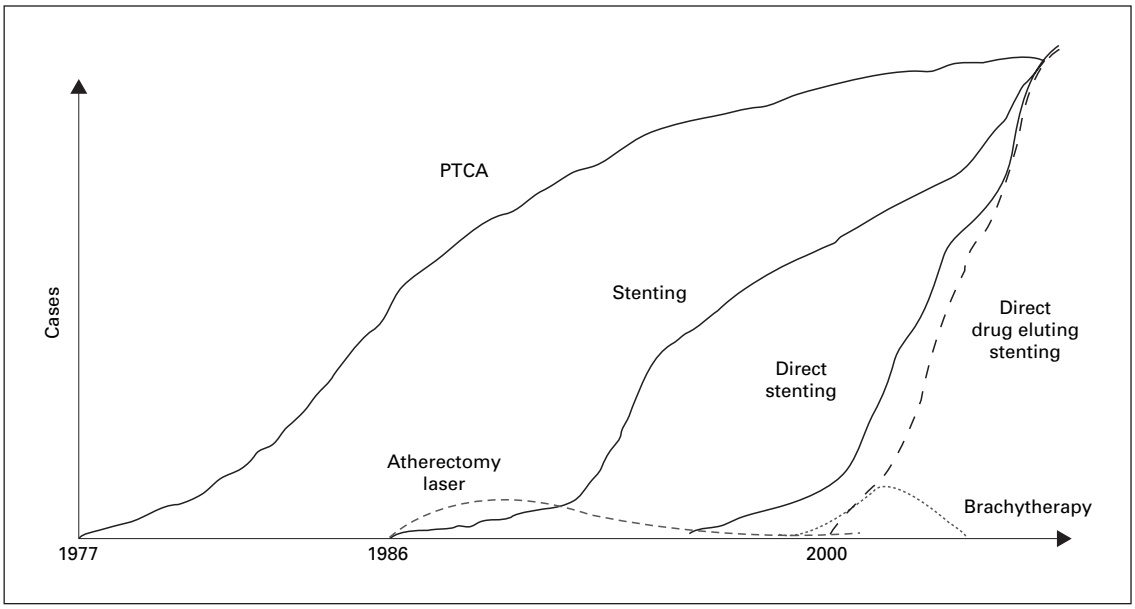

Fig. 10. Schematized evolution of PCI. The two valuable techniques [percutaneous transluminal coronary angioplasty (PTCA) often used today as a synonym for simple balloon angioplasty] and stenting prevail, although they had a more contained start than many of the alternative procedures such as various atherectomy and laser techniques, hailed in with bloated initial success reports but revealed not to be beneficial and most of the time even detrimental by larger scale registries or randomized trials. Brachytherapy for prevention of restenosis represents an exception as it was indeed effective. However, it fell victim to its small benefit compared with the investment (about 10 patients had to be irradiated to prevent 1 rehospitalization for a repeat intervention) and to the increasing use of the active stent, being at least much more simple if not more effective. On the other hand, even stenting (passive or active) is not used judiciously enough as outlined in the text. The current default procedure, direct drug-eluting stenting, promises a further increase in overall procedures that had plateaued more recently by treating more mild lesions.

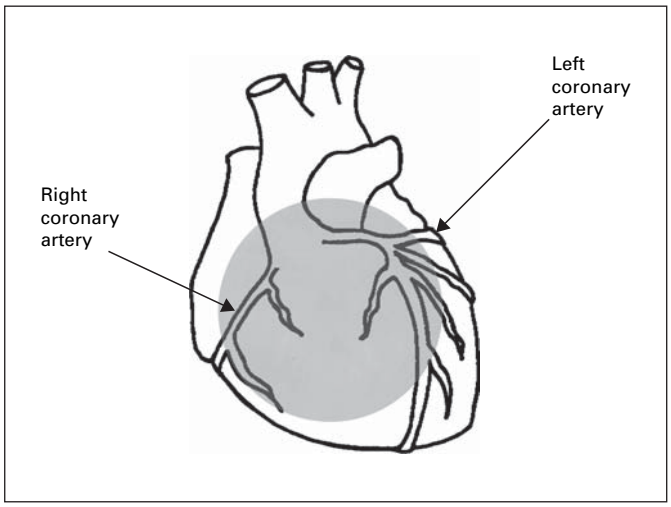

Fig. 11. Region of coronary arteries where plaque sealing (preventive balloon angioplasty of not yet hemodynamically significant stenoses) has been advocated [23].

nated by new generations of active stents or antiplatelet regimens.

Notwithstanding, the treatment of lesions before they become hemodynamically significant may be a good thing. After all, hemodynamic significance corresponds to symptoms more than to prognosis. Prognosis, on the other hand, is determined by plaque rupture and thrombosis of a coronary artery producing a myocardial infarction. Thus, the heretofore ubiquitously accepted principle of restricting PCI to hemodynamically significant lesions has been challenged [17], but it has not been waived yet. Hemodynamically nonsignificant stenoses account for the majority (about 80%) of myocardial infarctions [18–22] although their individual potential to cause an infarction is smaller than that of a hemodynamically significant stenosis. Plaque sealing by balloon angioplasty of such lesions in strategically important areas (fig. 11) has been advocated, based on the fact that balloon angioplasty carries virtually no risk of late thrombosis of the dilated site,

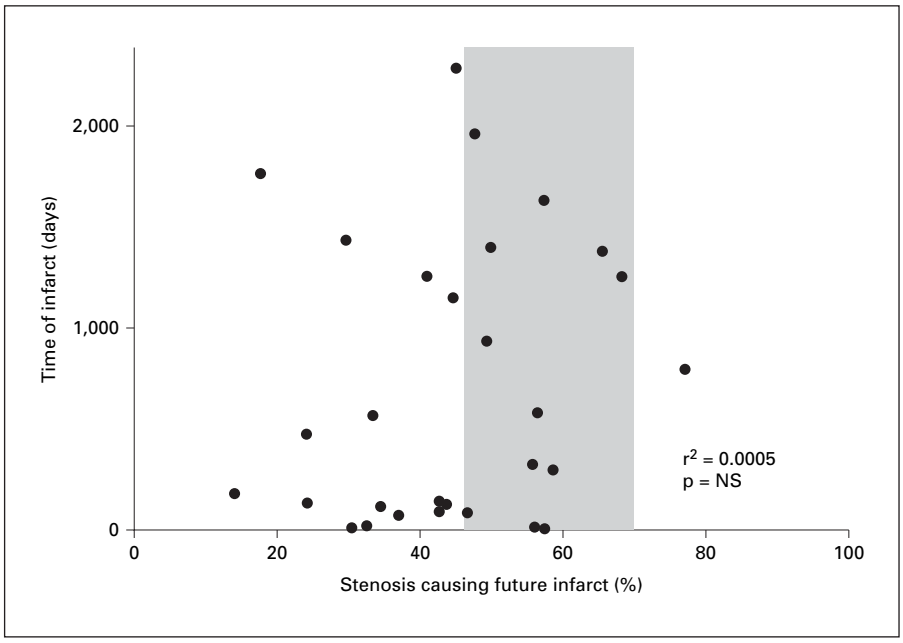

Fig. 12. Severity of stenosis and time of infarction occurring during follow-up after an initial coronary angiography [24]. The shaded area represents the degree of stenosis, where plaque sealing is recommended.

Table 2. Identification of vulnerable plaques

Intravascular ultrasound
Three-dimensional reconstruction
Ultrasound elastography (palpography)
Intravascular ultrasound flow velocity
Virtual histology
Angioscopy (direct visualization practically abandoned)
Optical coherence tomography
Raman (near infrared) spectroscopy
Thermography
Positron emission tomography
Computed tomography
Contrast
Ultrafast
Magnetic resonance
Phase contrast
Nuclear
Intravascular

even in the case of restenosis (which may cause angina but not infarction [23]), that hemodynamically nonsignificant stenoses harbor a low but significant risk of causing an infarction, and that it is not possible to predict which stenoses will rupture and when this will occur (fig. 12) [24].

Clearly, it would be best to predetermine the vulnerability of a hemodynamically nonsignificant stenosis before subjecting it to PCI. A variety of techniques are under clinical investigation (table 2). However, these methods are more apt to detect signs of vulnerability (thin cap plaque, fissure, incipient thrombosis) than to affirm stability, i.e. the adequacy of their specificity has not been demonstrated. Hence, it is likely that the use of one or several of these techniques will generally corroborate the indication for PCI, so that applying PCI without testing the plaque first would have been cheaper and quicker. Even in the rare instance where stability of the plaque has been confirmed by a number of these tests, this can only be regarded as a snap-shot assessment giving little information about the stability of the plaque during follow-up, not to mention the risk of having destabilized the plaque by using intra-arterial assessment devices. Short of a noninvasive test pinpointing vulnerable plaques and their precise locations from the outside, testing for vulnerability of plaques does not appear clinically rewarding.

On the other hand, the current policy of using (active) stents for all lesions makes plaque sealing far less appealing. The risk of spontaneous rupture of a nonhemodynamically significant plaque is about 1% per year given that mild lesions inherently are unlikely to rupture and that current treatments, widely applied, involving one or even two platelet inhibitors and a statin, generally reduce plaque activity and fragility. Insertion of a stent (passive or active) into a nonsevere stenosis carries a low but definite risk of subacute stent thrombosis. Even if that risk

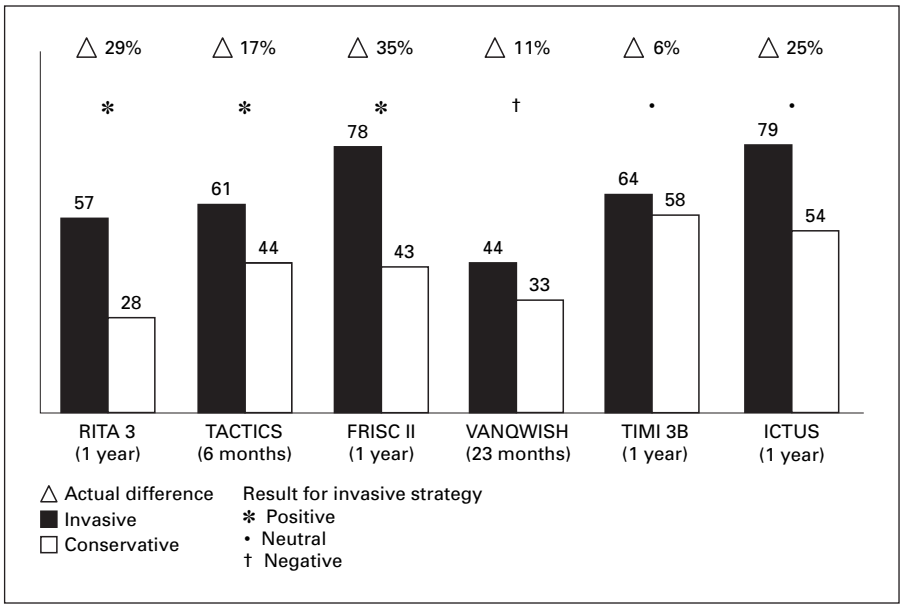

Fig. 13. Actual invasive revascularization in the invasive and conservative arms, respectively, of the randomized trials in patients with acute coronary syndrome. The difference was intended to be 100% but ranged from 6 to 35% only, significantly jeopardizing the power of detecting actual differences in outcome. Nevertheless, 3 studies were positive at the end of the follow-up period indicated in parentheses.

is estimated at 2% or less, this risk neutralizes a potential benefit at least for the first several years after the procedure. Regrettably, it would be unreasonable to believe that operators use stents judiciously (i.e. only when really needed because of a bad balloon result, which has to be expected in less than 40% with mild lesions); typically, operators feel compelled to treat a lesion with a less than clear indication for angioplasty by using a method believed to provide maximal procedural security (as perceived by the general operator) and minimal risk for restenosis. The fact that, without stenting, balloon angioplasty of a mild stenosis has a very low risk of abrupt closure, no risk of subacute closure, and only about a 10% risk of restenosis now appears to be forgotten or ignored.

Overall, PCI has never reached the status of a true life saving procedure, except when used for an acute myocardial infarction. In other acute coronary syndromes, its benefit over conservative treatment is limited to cases with ST segment deviation in more than 4 leads or of more than 3 mm (table 3) [25]. Results of trials randomizing patients with acute coronary syndromes between conservative and invasive treatments are mixed. One trial even demonstrated a disadvantage of the invasive therapy [26]. However, adherence to randomization has been poor in all trials, minimizing the confidence in conclusions from these studies, and the actual difference in the treatment carried out was only 6–25% in the neutral or negative trials (fig. 13). A meta-analysis of almost 10,000 patients with acute coronary syndrome, randomized between invasive and conservative therapy, shows that the in-hospital disadvantage in terms of mortality and myocardial infarction of the invasive treatment arm was more than compensated for during follow-up, resulting in a overall benefit for the invasive arm (fig. 14).

The trial with the longest follow-up (RITA 3) took 5 years to demonstrate the superiority of invasive intervention in terms of mortality or myocardial infarction [27] (fig. 15). In the recently published ICTUS trial of 1,200

Table 3. Risk of reduced cardiac events in patients with unstable angina pectoris randomized to invasive or conservative therapy according to ECG criteria [25]

ST segment deviation	Conservative strategy %	Invasive strategy %	Relative risk of death or myocardial infarction, %	Adjusted odds ratio[a] %
0–4 leads	9.1	10.0	1.09	1.13
5–7 leads	15.7	8.8	0.51	0.45
≥8 leads	19.2	8.5	0.44	0.36
0–2.5 mm	9.3	11.8	1.25	1.26
3.0–5.5 mm	13.3	6.2	0.46	0.42
≥6.0 mm	19.4	9.5	0.49	0.41

[a] Data from the FRISC II trial adjusted for age, gender, previous infarction, diabetes, hypertension, smoking status, and troponin T.

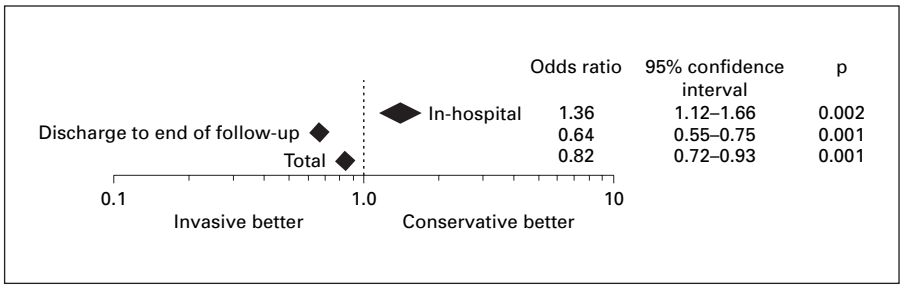

Fig. 14. Risk concerning mortality and myocardial infarction of 9,200 patients with acute coronary syndrome of 7 randomized trials between invasive and conservative treatment (FRISC II, MAT, TIMI IIIB, TACTICS, VANQWISH, RITA 3). The in-hospital disadvantage of invasive therapy is converted to an overall benefit by a better course after hospital discharge.

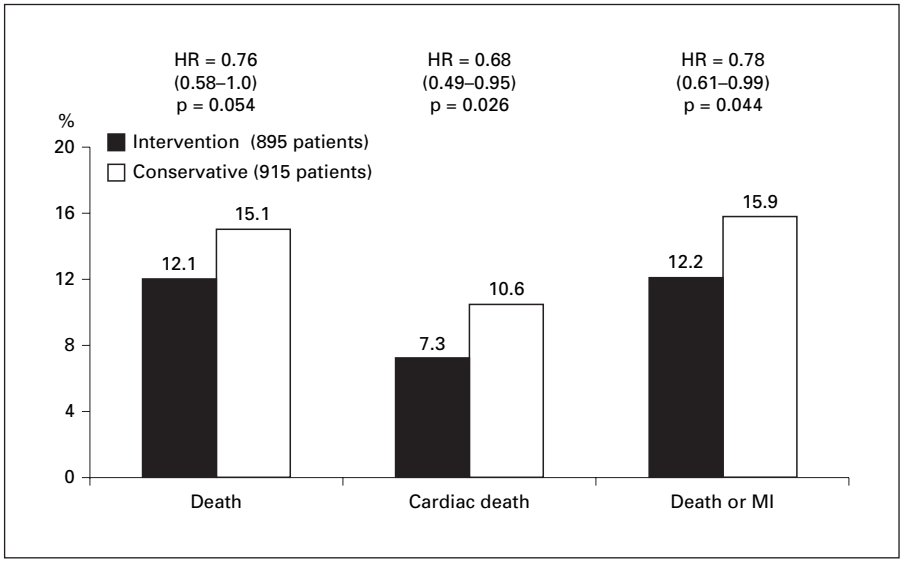

Fig. 15. Outcome at 5 years in the RITA 3 trial [27] in patients with non-ST elevation acute coronary syndrome. HR = Hazard ratio; MI = myocardial infarction.

patients randomized between invasive or selective treatment for troponin-positive acute coronary syndrome with 100% use of abciximab, a glycoprotein IIb/IIIa inhibitor, there was absolutely no benefit of the invasive therapy at 1 year [28] in terms of pooled major adverse cardiac events, including rehospitalization, which does not preclude a later benefit.

In all comers, elective PCI shows no evidence of benefit in terms of prognostic endpoints (death or myocardial infarction) compared with conservative treatment [29]. Regarding nonfatal infarction and need for repeat intervention, there was even a suggestion that the invasive strategy is inferior. Similar results were published in a trial randomizing patients with significant single-vessel disease to PCI or an exercise program [30].

It is understandable that interventional cardiologists do not get discouraged by such data and continue to offer PCI to their patients. The option to get rid of angina and of having the problem resolved with a catheter intervention is appealing to patients and their consent is invariably forthcoming.

It is more difficult to defend offering PCI to patients with double- or triple-vessel disease, based on concerns for survival, after the publication of the results of a New York registry clearly showing that survival is better with bypass surgery than with PCI, even in double-vessel disease without involvement of the left anterior descending coronary artery [31]. While this appears trivial for patients with severe triple-vessel disease or those with involvement of the left main stem, the finding that patients with double-vessel disease should not undergo PCI because of an increased mortality compared with bypass surgery comes as a surprise, even when acknowledging that patients with acute myocardial infarction were excluded. Once again, interventional cardiologists ignore data that do not corroborate their common beliefs; this may or may not be beneficial for the patients.

Looking at all randomized studies comparing PCI and CABG in multivessel disease, mortality was favorable in one trial each for CABG and PCI and not significantly different in the remainder or the pooled data [32] (fig. 16). In all these trials there was a distinct advantage for CABG

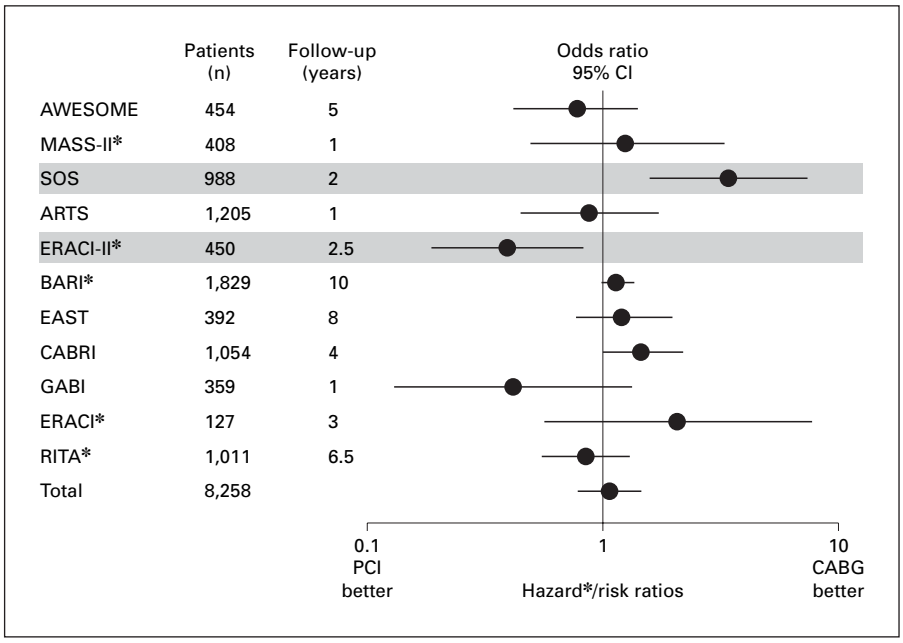

Fig. 16. Mortality risk in trials randomizing elective patients (most with multivessel disease) between PCI (with or without stenting) and CABG. The shaded trials showed a significant advantage, one for each of the treatment modalities [modified from 32].

regarding the need for reinterventions. The currently ongoing trials randomizing patients to PCI with active stents or to CABG may indicate a reduction of the difference. Yet they are unlikely to eliminate it, and will hardly impact on the difference in prognostic endpoints such as mortality or infarction.

In summary, PCI is a potent, user-friendly, and relatively innocuous treatment modality for coronary revascularization. In the numbers of patients treated, it has outstripped CABG by a factor of 2 to 4, mainly due to timelier and better screening for early disease, easier accessibility of PCI, and a well-established self-referral pattern of interventional cardiologists who also perform the diagnostic coronary angiogram. To date it is preferably carried out as an ad hoc procedure (diagnostic and therapeutic catheterization in one session) and it almost invariably involves stenting, with the use of active stents quickly becoming the rule. There are no data to support the unconditional use of stenting, the preference of PCI over conservative treatment in stable single-vessel disease, or the use of PCI rather than CABG for multivessel disease. Hints that a conservative treatment, taking advantage of the demonstrated efficacy of modern drugs for secondary prevention and the apparent adjunctive benefit of active lifestyle coaching [29, 30], might be superior to PCI or that mortality is reduced when double-vessel disease is treated with CABG rather than PCI [31] are ignored to maintain the dominant position of PCI treasured by patients and physicians (with the exception, perhaps, of cardiac surgeons). This somewhat irrational behavior is germane to all medical disciplines and, therefore, cannot be condemned.

Table 4. PCI armamentarium 2006

Standard	Optional
Improved balloons	Atherectomy
Improved guide wires	Drills, grinders, suckers
Improved guide catheters	Lysers, softeners, catchers
	Laser (debulker/wire)
Stents (drug eluting)	Local drug delivery
ADP + GP IIb/IIIa antagonists	Drugs for restenosis
	IVUS (2D/3D/Doppler)
Femoral plugs + sutures	Pressure wire
Digital X-ray	Angioscopy
	Distal protection devices
	Brachytherapy
	Percutaneous LV assist devices
	Percutaneous CPS

ADP = Adenosine diphosphate; CPS = cardiopulmonary support; D = dimensional; GP = glycoprotein; LV = left ventricular; IVUS = intravascular ultrasound.

Table 4 indicates what is necessary (standard) and what is optional for performing PCI today.

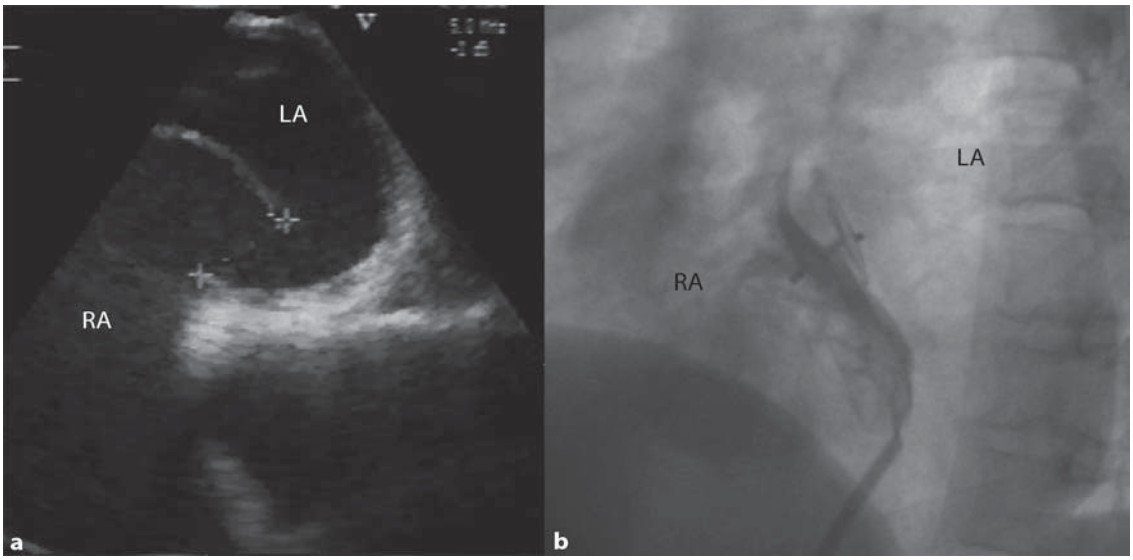

Fig. 17. a Transesophageal echocardiography in a 39-year-old mother of 2 teenage sons. The patient permanently lost the capacity of speech because of a paradoxical cerebral insult. The patent foramen ovale is indicated between the 2 crosses. **b** Angiogram after device closure with a 25-mm Amplatzer PFO occluder. The intervention took less than 15 min under local anesthesia. It should have been performed before the devastating stroke had occurred. LA = Left atrium; RA = right atrium.

Noncoronary Interventions

Closure of the patent foramen ovale is the one procedure capable of challenging the dominant role of coronary angioplasty [33] as the most frequently performed interventional procedure. Recurrence of paradoxical embolism can be reliably prevented by closing the patent foramen ovale. This can be accomplished with an Amplatzer PFO occluder (currently the device of choice) in less than 15 min with a procedure virtually free of complications, need for aftercare, or temporary disability. The fact that the patient can get up 1 h after the intervention carried out under local anesthesia through a puncture of the femoral vein and go about any business he or she likes (including sports) without any waiting period is appealing to patients who had a stroke or where there is a risk of a stroke. It is even appealing to deep sea divers and patients suffering from migraine, although the preventive potential (fewer diving incidents or migraine attacks, respectively) of the closure of the patent foramen ovale in these patients is less well documented. A compelling case like the one shown in figure 17 argues in favor of screening people in young adulthood for a large patent foramen ovale with a mobile septum primum (atrial septal aneurysm), before they fall victim to a possibly disabling stroke having a terrible effect on the rest of their often long lives.

This still controversial position is supported by a large autopsy series showing that the prevalence of a patent foramen ovale decreases from young to old people. This suggests a selective mortality rather than the unlikely mechanism (proposed by the authors) of spontaneous closure of the foramen ovale with advancing age [34].

Similar techniques have been proposed to exclude the left atrial appendage in patients with atrial fibrillation [35, 36]. If the technique can be simplified and rendered safer (with current devices, the risk of cardiac perforation or device embolization is considerable), and if it is found that efficacy parallels or exceeds that of oral anticoagulation, this approach could become as common as coronary angioplasty in very elderly people, where the prevalence of atrial fibrillation approaches 20%. As mentioned earlier, the same potential for growth in numbers of patients treated exists for radiofrequency ablation for atrial fibrillation.

Finally, promising catheter-based, percutaneous techniques to replace stenotic (or insufficient) aortic or pulmonic valves, or to ameliorate mitral regurgitation after a myocardial infarction, or in the context of a dilated left ventricle may also become commonplace interventions. However, these methods need to be perfected before they can become widely used. Aortic stenosis in the elderly is

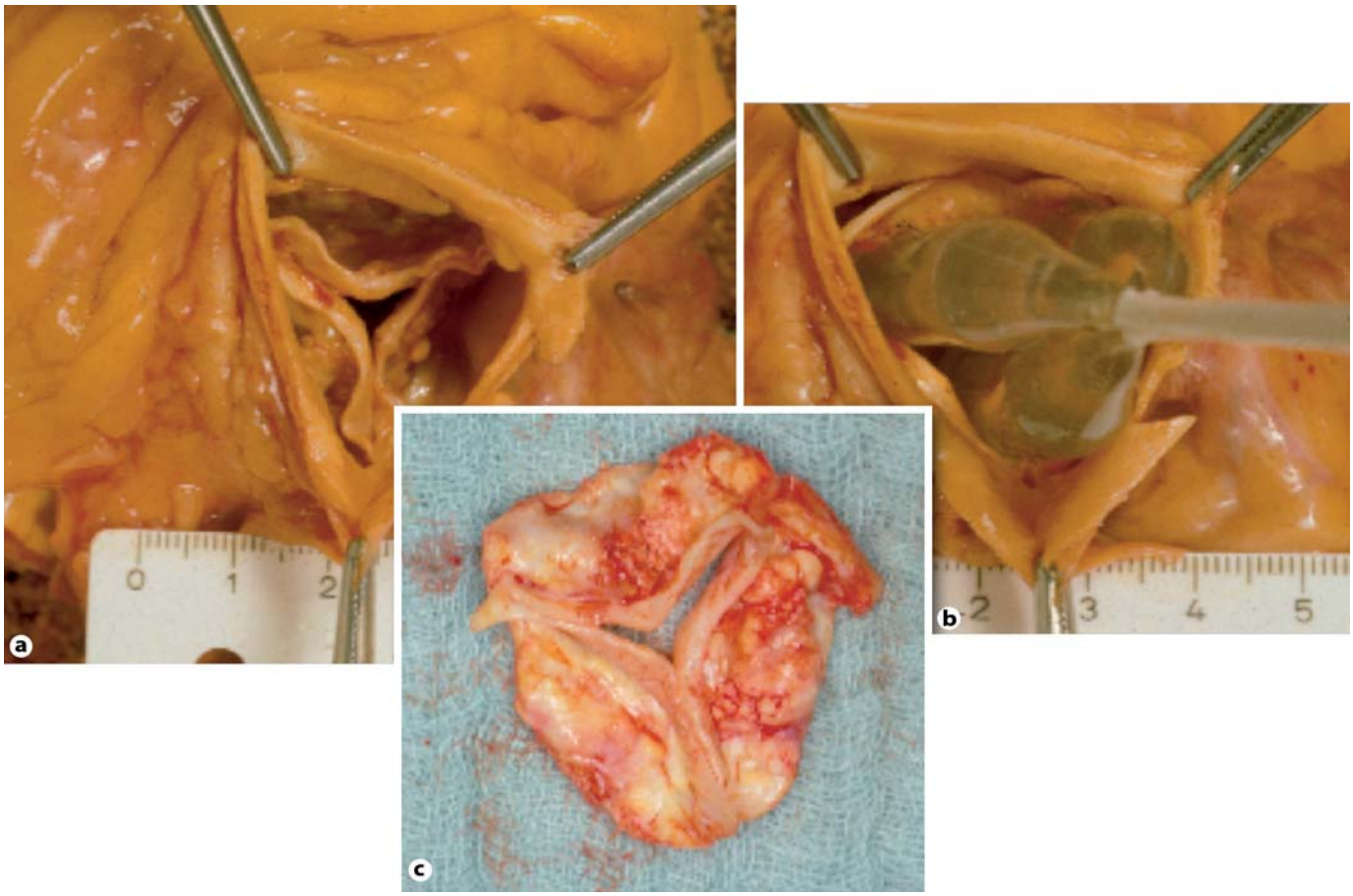

Fig. 18. Balloon angioplasty of a severe senile aortic valve stenosis. **a** Situation before balloon insertion with heavy calcifications of the thickened leaflets but normally separated commissures. **b** A 3 × 12 mm Trefoil balloon is inserted for valvuloplasty. It opens the valve without inducing any anatomic change. **c** Removed valve after a futile balloon valvuloplasty (patient received an artificial valve, currently still the only valuable therapy for this disease).

a particularly frequent problem for which balloon valvuloplasty simply has never been successful at all, much in contrast to what has been published over the years (fig. 18).

Future Directions

Injection of stem cells and gene factors has shown some encouraging results in patients with occluded peripheral and coronary vessels and infarcted myocardium. Nonetheless, it is unlikely that this intriguing addition to interventional cardiology will mature into a routine method within the next decades (or ever).

In the western world, interventional cardiology has grown to one of the most important disciplines in medicine. It has the formidable capacity to improve the quality of life and longevity as well as for innovation, employment, scientific activities, and social gatherings. Interventional cardiologists behave like other professionals. They gather information and subconsciously select what is best suited to their purposes and convictions, largely ignoring the remainder. Where no data are available, they follow their instinct and personal experience along with the saying 'lack of proof of evidence is not proof of lack of evidence'. As most interventional cardiologists, like other doctors, are caring persons, there is not much wrong with this.

References

1 Garrison F: On Thomas Sydenham (1624–1689). Bull NY Acad Med 1928;4:993.
2 Rubio-Alvarez V, Larson RL, Soni J: Valvulotomias intracardiacas por medio de un cateter. Arch Inst Cardiol Mex 1953;23:183–192.
3 Rashkind WJ, Miller WW: Creation of an atrial septal defect without thoracotomy. JAMA 1966;196:991–992.
4 Porstmann W, Wierny L, Warnke H: Der Verschluss der Ductus arteriosus persistens ohne Thorakotomie. Thoraxchirurgie 1967;15:199–203.
5 King TD, Thompson SL, Steiner C, Mills NL: Secundum atrial septal defect. Nonoperative closure during cardiac catheterization. JAMA 1976;235:2506–2509.
6 Anderson JH, Wallace S, Gianturco C, Gerson LP: 'Mini' Gianturco stainless steel coils for transcatheter vascular occlusion. Radiology 1979;132:301–303.
7 Gruentzig AR: Transluminal dilatation of coronary-artery stenosis. Lancet 1978;i:263.
8 Meier B: The first patient to undergo coronary angioplasty, 23-year follow-up. N Engl J Med 2001;344:144–145.
9 Gallagher JJ, Svenson RH, Kasell JH, German LD, Bardy GH, Broughton A, Critelli G: Catheter technique for closed-chest ablation of the atrioventricular conduction system. N Engl J Med 1982;306:194–200.
10 Bridges ND, Hellenbrand W, Latson L, Filiano J, Newburger JW, Lock JE: Transcatheter closure of patent foramen ovale after presumed paradoxical embolism. Circulation 1992;86:1902–1908.
11 Cook S, Togni M, Walpoth N, Maier W, Muehlberger V, Legrand V, Milicic D, Zambartas C, Zeliko M, Madsen J, van Buuren F, Lòpez-Palop R, Peeba M, Koskenkorva J, Vanhanen H, Lablanche JM, Lazaris I, Géza F, Eyjolfsson K, Kearney P, Piscione F, Erglis A, Navickas R, Beissel J, Chanman I, Fridrich V, Zorman D, Nilsson T, Oezman F, Ludman P, Meier B: Percutaneous coronary interventions in Europe 1992–2003. Eurointervention, in press.
12 Puel J, Joffre F, Rousseau H, Guermonprez B, Lancelin B, Valeix B, Imbert G, Bounhoure JP: Endo-prothèses coronariennes auto-expansives dans la prévention des resténoses après angioplastie transluminale. Arch Mal Coeur Vaiss 1987;80:1311–1312.
13 Detre KM, Holmes DR Jr, Holubkov R, Cowley MJ, Bourassa MG, Faxon DP, Dorros GR, Bentivoglio LG, Kent KM, Myler RK, Kellett MA, Sanborn T, Jacobs AK, Erario M, King SBI, Douglas J, Sutor C, Ewels C, Kehoe K: Incidence and consequences of periprocedural occlusion. The 1985–1986 National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry. Circulation 1990;82:739–750.
14 Schomig A, Kastrati A, Mudra H, Blasini R, Schuhlen H, Klauss V, Richardt G, Neumann FJ: Four-year experience with Palmaz-Schatz stenting in coronary angioplasty complicated by dissection with threatened or present vessel closure. Circulation 1994;90:2716–2724.
15 Brophy JM, Belisle P, Joseph L: Evidence for use of coronary stents. A hierarchical bayesian meta-analysis. Ann Intern Med 2003;138:777–786.
16 Babapulle MN, Joseph L, Belisle P, Brophy JM, Eisenberg MJ: A hierarchical Bayesian meta-analysis of randomised clinical trials of drug-eluting stents. Lancet 2004;364:583–591.
17 Meier B, Ramamurthy S: Plaque sealing by coronary angioplasty. Catheter Cardiovasc Diagn 1995;36:295–297.
18 Nobuyoshi M, Kimura T, Ohishi H, Horiuchi H, Nosaka H, Hamasaki N, Yokoi H, Kim K: Restenosis after percutaneous transluminal coronary angioplasty: pathologic observations in 20 patients. J Am Coll Cardiol 1991;17:433–439.
19 Alderman EL, Corley SD, Fisher LD, Chaitman BR, Faxon DP, Foster ED, Killip T, Sosa JA, Bourassa MG: Five-year angiographic follow-up of factors associated with progression of coronary artery disease in the Coronary Artery Surgery Study (CASS). CASS Participating Investigators and Staff. J Am Coll Cardiol 1993;22:1141–1154.
20 Abizaid AS, Mintz GS, Mehran R, Abizaid A, Lansky AJ, Pichard AD, Satler LF, Wu H, Pappas C, Kent KM, Leon MB: Long-term follow-up after percutaneous transluminal coronary angioplasty was not performed based on intravascular ultrasound findings: importance of lumen dimensions. Circulation 1999;100:256–261.
21 Qiao JH, Fishbein MC: The severity of coronary atherosclerosis at sites of plaque rupture with occlusive thrombosis. J Am Coll Cardiol 1991;17:1138–1142.
22 Falk E, Shah PK, Fuster V: Coronary plaque disruption. Circulation 1995;92:657–671.
23 Meier B, Ramamurthy S: Plaque sealing by coronary angioplasty. Catheter Cardiovasc Diagn 1995;36:295–297.
24 Little WC, Constantinescu M, Applegate RJ, Kutcher MA, Burrows MT, Kahl FR, Santamore WP: Can coronary angiography predict the site of a subsequent myocardial infarction in patients with mild-to-moderate coronary artery disease? Circulation 1988;78:1157–1166.
25 Holmvang L, Clemmensen P, Lindahl B, Lagerqvist B, Venge P, Wagner G, Wallentin L, Grande P: Quantitative analysis of the admission electrocardiogram identifies patients with unstable coronary artery disease who benefit the most from early invasive treatment. J Am Coll Cardiol 2003;41:905–915.
26 Boden WE, O'Rourke RA, Crawford MH, Blaustein AS, Deedwania PC, Zoble RG, Wexler LF, Kleiger RE, Pepine CJ, Ferry DR, Chow BK, Lavori PW: Outcomes in patients with acute non-Q-wave myocardial infarction randomly assigned to an invasive as compared with a conservative management strategy. Veterans Affairs Non-Q-Wave Infarction Strategies in Hospital (VANQWISH) Trial Investigators. N Engl J Med 1998;338:1785–1792.
27 Fox KA, Poole-Wilson P, Clayton TC, Henderson RA, Shaw TR, Wheatley DJ, Knight R, Pocock SJ: Five-year outcome of an interventional strategy in non-ST-elevation acute coronary syndrome: the British Heart Foundation RITA 3 randomised trial. Lancet 2005;366:914–920.
28 De Winter RJ, Windhausen F, Cornel JH, Dunselman PH, Janus CL, Bendermacher PE, Michels HR, Sanders GT, Tijssen JG, Verheugt FW: Early invasive versus selectively invasive management for acute coronary syndromes. N Engl J Med 2005;353:1095–1104.
29 Katritsis DG, Ioannidis JP: Percutaneous coronary intervention versus conservative therapy in nonacute coronary artery disease: a meta-analysis. Circulation 2005;111:2906–2912.
30 Hambrecht R, Walther C, Mobius-Winkler S, Gielen S, Linke A, Conradi K, Erbs S, Kluge R, Kendziorra K, Sabri O, Sick P, Schuler G: Percutaneous coronary angioplasty compared with exercise training in patients with stable coronary artery disease: a randomized trial. Circulation 2004;109:1371–1378.
31 Hannan EL, Racz MJ, Walford G, Jones RH, Ryan TJ, Bennett E, Culliford AT, Isom OW, Gold JP, Rose EA: Long-term outcomes of coronary-artery bypass grafting versus stent implantation. N Engl J Med 2005;352:2174–2183.
32 Best PJ, Berger PB: Can percutaneous coronary interventions reduce death and myocardial infarction in stable and unstable coronary disease? Catheter Cardiovasc Interv 2004;61:528–536.
33 Meier B: Closure of patent foramen ovale: technique, pitfalls, complications, and follow up. Heart 2005;91:444–448.
34 Hagen PT, Scholz DG, Edwards WD: Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. Mayo Clin Proc 1984;59:17–20.
35 Sievert H, Lesh MD, Trepels T, Omran H, Bartorelli A, Della Bella P, Nakai T, Reisman M, DiMario C, Block P, Kramer P, Fleschenberg D, Krumsdorf U, Scherer D: Percutaneous left atrial appendage transcatheter occlusion to prevent stroke in high-risk patients with atrial fibrillation: early clinical experience. Circulation 2002;105:1887–1889.
36 Meier B, Palacios I, Windecker S, Rotter M, Cao QL, Keane D, Ruiz CE, Hijazi ZM: Transcatheter left atrial appendage occlusion with Amplatzer devices to obviate anticoagulation in patients with atrial fibrillation. Catheter Cardiovasc Interv 2003;60:417–422.